Notice of Allowability

Application No.	Applicant(s)
09/627,775	Greene
Examiner	**Art Unit**
Arun Chakrabarti	1634

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *6/4/03*.

2. ☒ The allowed claim(s) is/are *2, 3, 5-16, 18-30, 34, 35, and 37-48*.

3. ☒ The drawings filed on *Jul 28, 2000* are accepted by the Examiner.

4. ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

   a) ☐ All b) ☐ Some* c) ☐ None of the:

   1. ☐ Certified copies of the priority documents have been received.
   2. ☐ Certified copies of the priority documents have been received in Application No. _____.
   3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   *Certified copies not received: _____.

5. ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

   (a) ☐ The translation of the foreign language provisional application has been received.

6. ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS must be submitted.

   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached

   1) ☐ hereto or 2) ☐ to Paper No. _____.

   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the examiner.

   (c) ☐ including changes required by the attached Examiner's Amendment/Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

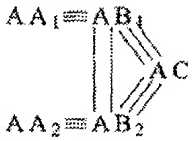
Attachment(s)

1 ☐ Notice of References Cited (PTO-892)
2 ☐ Notice of Informal Patent Application (PTO-152)
3 ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
4 ☒ Interview Summary (PTO-413), Paper No. *0603*.
5 ☐ Information Disclosure Statement(s) (PTO-1449), Paper No(s). _____
6 ☒ Examiner's Amendment/Comment
7 ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
8 ☒ Examiner's Statement of Reasons for Allowance
9 ☐ Other

Claimspto / 1634

C. Dessau

Claim 2 **(Amended)** A method of inhibiting osteoclastogenesis comprising the step of administering to a patient an amount of an inhibitor effective to inhibit osteoclastogenesis, wherein the inhibitor has the formula:



(I)

wherein:

AC is a peptide of 3-18 amino acid residues which corresponds in primary sequence to a binding loop of a TNF-R superfamily member, and which may optionally contain one or more amino acid substitutions, or an analogue thereof wherein at least one amide linkage is replaced with a substituted amide or an isostere of amide;

AB_1 is a moiety having a first functional group capable of forming a covalent linkage with one terminus of AC, a second functional group capable of forming a covalent linkage with AB_2 and a third functional group capable of forming a covalent linkage with AA_1 ;

AB_2 is a moiety having a first functional group capable of forming a covalent linkage with the second terminus of AC, a second functional group capable of forming a covalent linkage with AB_1 and a third functional group capable of forming a covalent linkage with AA_2;

AA_1 is a moiety having hydrophobic properties and a functional group capable of forming a covalent linkage with the third functional group of AB_2;

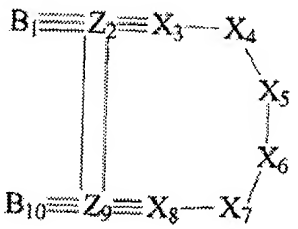
AA_2 is a moiety having hydrophobic properties and a functional group capable of forming a covalent linkage with the third functional group of AB_2;

"═" is a covalent linkage; and

"≡" is a covalent linkage.

3. The method of Claim 2 in which the amino acid substitutions are conservative.

5. (Amended) The method of Claim 4 wherein the inhibitor has the formula:



(II)

wherein:

B_1 and B_{10} are each independently a peptide of 1-6 amino acids at least one of which os a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_2 is a moiety forming a covalent linkage with B_1 , X_3 and Z_9;

Z_9 is a moiety forming a covalent linkage with B_{10}, X_8 and Z_2;

X_3 is absent or a hydrophilic amino acid;

X_4 is a hydrophobic amino acid;

X_5 is a hydrophobic amino acid;

X_6 is a hydrophobic amino acid;

X_7 is a hydrophobic or hydrophilic amino acid;

X_8 is a hydrophobic or hydrophilic amino acid;

"-" is an amide, substituted amide or an isostere of amide thereof;

"$=$" is a covalent linkage; and

"$\equiv$" is a covalent linkage.

6. The method of Claim ~~5~~, wherein:

B_1 and B_{10} are each independently a peptide of 1-2 amino acids, at least one of which is an aromatic amino acid ;

Z_2 and Z_9 are each independently a Cys-like amino acid;

X_3 is absent or an acidic amino acid;

X_4 is an aromatic or apolar amino acid;

X_5 is a polar amino acid;

X_6 is a polar amino acid;

X_7 is an aromatic or polar amino acid;

X_8 is an aromatic, apolar or polar amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

6. The method of Claim 5, wherein:

B_1 and B_{10} are each independently Tyr or Phe;

Z_2 and Z_9 are each Cys;

X_3 is absent or Glu;

X_4 is Trp or Leu;

X_5 is Ser;

X_6 is Gln;

X_7 is Tyr or Asn;

X_8 is Tyr or Leu;

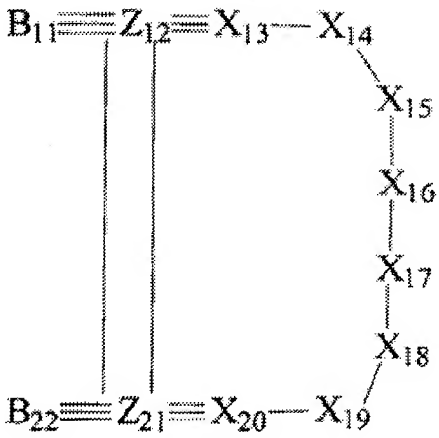
"-" is an amide linkage;

"═" is a disulfide linkage; and

"≡" is an amide linkage.

8. The method of Claim 7, wherein said inhibitor is selected from the group consisting of WP9Q - SEQ ID NO:13, WP9ELY - SEQ ID NO:12, WP9Y - SEQ ID NO:14, and WP9QY - SEQ ID NO:15.

9. (Amended) The method of Claim 4, wherein the inhibitor has the formula:

(III) 

wherein:

B_{11} and B_{22} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_{12} is a moiety forming a covalent linkage with B_{11}, X_{13} and Z_{21};

Z_{21} is a moiety forming a covalent linkage with B_{22}, X_{20} and Z_{12};

X_{13} is absent or hydrophobic amino acid;

X_{14} is absent or hydrophilic amino acid;

X_{15} is a hydrophilic or hydrophobic amino acid;

X_{16} is a hydrophilic amino acid;

X_{17} is absent or a hydrophobic amino acid;

X_{18} is a hydrophilic amino acid;

X_{19} is a hydrophilic amino acid;

X_{20} is a hydrophilic amino acid;

"-" is an amide, a substituted amide or an isostere of amide thereof;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

10. The method of Claim 9, wherein:

B_{11} and B_{22} are each independently a peptide of 1-3 amino acids, at least one of which is an aromatic amino acid;

Z_{12} and Z_{21} are each independently a Cys-like amino acid;

X_{13} is absent or an aromatic amino acid;

X_{14} is absent or a polar amino acid;

X_{15} is a basic, polar or apolar amino acid;

X_{16} is a polar amino acid;

X_{17} is absent or an apolar amino acid;

X_{18} is an acidic amino acid;

X_{19} is a polar amino acid;

X_{20} is a basic amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

11. The method of Claim 10, wherein:

B_{11} and B_{22} are each independently Tyr or Phe;

Z_{12} and Z_{21} are each Cys;

X_{13} is absent or Phe;

X_{14} is absent or Thr;

X_{15} is Ala, Asn or Arg;

X_{16} is Ser;

X_{17} is absent or Val;

X_{18} is Glu;

X_{19} is Asn;

X_{20} is Arg or His;

"-" is an amide linkage;

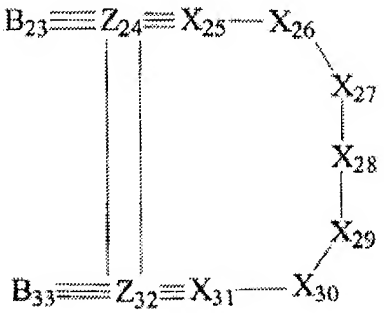
"=" is a disulfide linkage; and

"≡" is an amide linkage.

12. The method of Claim 11, wherein said inhibitor is selected from the group consisting of WP5 - SEQ ID NO:16, WP5N - SEQ ID NO:17, WP5R - SEQ ID NO:18, WP5J - SEQ ID NO:19, WP5JY - SEQ ID NO:20, WP5JN - SEQ ID NO:21, WP5JR - SEQ ID NO:22, and WP5VR - SEQ ID NO:23.

13. (Amended) The method of Claim 4, wherein the inhibitor has the formula:

(IV)



B_{23} and B_{33} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_{24} is a moiety forming a covalent linkage with B_{23}, X_{25} and Z_{32};

Z_{32} is a moiety forming a covalent linkage with B_{33}, X_{31} and Z_{24};

X_{25} is absent or a hydrophilic amino acid;

X_{26} is a hydrophilic amino acid;

X_{27} is a hydrophilic amino acid;

X_{28} is a hydrophilic amino acid;

X_{29} is a hydrophilic amino acid;

X_{30} is absent or a hydrophilic amino acid;

X_{31} is absent or a hydrophilic amino acid;

"-" is an amide, a substituted amide or an isostere of amide;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

14. The method of Claim 13, wherein:

B_{23} and B_{33} are each independently a peptide of 1-3 amino acids, at least one of which is an aromatic amino acid;

Z_{24} and Z_{32} are each independently a Cys-like amino acid;

X_{25} is absent or a basic amino acid;

X_{26} is a basic amino acid;

X_{27} is an acidic amino acid;

X_{28} is an apolar amino acid;

X_{29} is an apolar amino acid;

X_{30} is absent or a polar amino acid;

X_{31} is absent or an apolar amino acid;

"-" is an amide linkage'

"=" is a disulfide linkage; and

"≡" is an amide linkage.

15. (Amended) The method of Claim 14, wherein:

B_{23} and B_{33} are each independently Tyr or Phe;

Z_{24} and Z_{32} are each Cys;

X_{25} is absent or Arg;

X_{26} is Lys;

X_{27} is Glu;

X_{28} is Leu, Pro or Met;

X_{29} is Gly;

X_{30} is absent or Gln;

X_{31} is absent or Val;

"-" is an amide linkage;

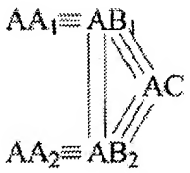
" = " is a disulfide linkage; and

" ≡ " is an amide linkage.

16. The method of Claim 15, wherein said inhibitor is selected from the group consisting of WP8L - SEQ ID NO:24, WP8JP - SEQ ID NO:25, WP8J - SEQ ID NO:26, and WP8JF - SEQ ID NO:27.

17. A method of treating patients who have diseases characterized by bone loss comprising the step of administering to said patient an amount of an inhibitor effective to inhibit such bone loss.

18. (Twice amended) A method of treating patients who have diseases characterized by bone loss comprising the step of administering to said patient an amount of an inhibitor effective to inhibit such bone loss, wherein said inhibitor is a compound having the formula:



(I)

wherein:

AC is a peptide of 3-18 amino acid residues which corresponds in primary sequence to a binding loop of TNF-R(I), and which may optionally contain one or more amino acid substitutions, or an analogue thereof wherein at least one amide linkage is replaced with a substituted amide or an isostere of amide;

AB_1 is a moiety having a first functional group forming a covalent linkage with one terminus of AC, a second functional group forming a covalent linkage with AB_2 and a third functional group forming a covalent linkage with AA_1;

AB_2 is a moiety having a first functional group forming a covalent linkage with the second terminus of AC, a second functional group forming a covalent linkage with AB_1 and a third functional group forming a covalent linkage with AA_2;

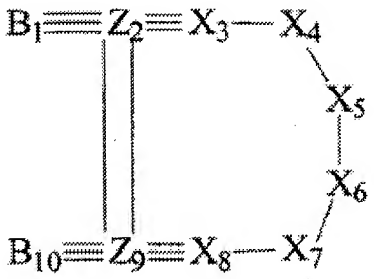
AA_1 is a moiety having hydrophobic properties and a functional group forming a covalent linkage with the third functional group of AB_1;

AA_2 is a moiety having hydrophobic properties and a functional group forming a covalent linkage with the third functional group of AB_2;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

19. (Amended) The method of claim 18 wherein the compound has the formula:



(II)

wherein:

B_1 and B_{10} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_2 is a moiety that is forming a covalent linkage with B_1, X_3 and Z_9;

Z_9 is a moiety that is forming a covalent linkage with B_{10}, X_8 and Z_2;

X_3 is absent or a hydrophilic amino acid;

X_4 is a hydrophobic amino acid;

X_5 is a hydrophilic amino acid;

X_6 is a hydrophilic amino acid;

X_7 is a hydrophobic or hydrophilic amino acid;

X_8 is a hydrophobic or hydrophilic amino acid;

"-" is an amide, substituted amide or an isostere of amide thereof;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

20. The method of claim 19 wherein:

B_1 and B_{10} are each independently a peptide of 1-3 amino acids, at least one of which is an aromatic amino acid;

Z_2 and Z_9 are each independently a Cys-like amino acid;

X_3 is absent or an acidic amino acid;

X_4 is an aromatic or apolar amino acid;

X_5 is a polar amino acid;

X_6 is a polar amino acid;

X_7 is an aromatic or polar amino acid;

X_8 is an aromatic, apolar or polar amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

21. The method of claim 20 wherein:

B_1 and B_{10} are each independently Tyr or Phe;

Z_2 and Z_9 are each Cys;

X_3 is absent or Glu;

X_4 is Trp or Leu;

X_5 is Ser;

X_6 is Gln;

X_7 is Tyr or Asn;

X_8 is Tyr or Leu;

"-" is an amide linkage;

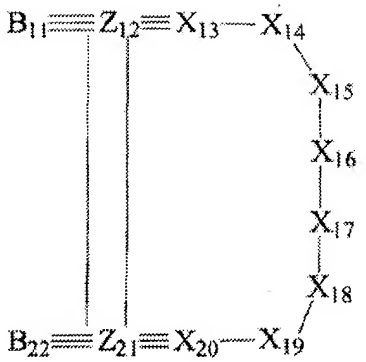
"═" is a disulfide linkage; and

"≡" is an amide linkage.

22. The method of claim 18 wherein the compound is selected from the group consisting of WP9Q - SEQ ID NO: 13, WP9ELY - SEQ ID NO: 12, WP9Y - SEQ ID NO: 14, and WP9QY - SEQ ID NO: 15.

23. (Amended) The method of claim 18 wherein the compound has the formula:

(III)



wherein:

B_{11} and B_{22} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_{12} is a moiety forming a covalent linkage with B_{11}, X_{13} and Z_{21};

Z_{21} is a moiety forming a covalent linkage with B_{22}, X_{20} and Z_{12};

X_{13} is absent or hydrophobic amino acid;

X_{14} is absent or a hydrophilic amino acid;

X_{15} is a hydrophilic or hydrophobic amino acid;

X_{16} is a hydrophilic amino acid;

X_{17} is absent or a hydrophobic amino acid;

X_{18} is a hydrophilic amino acid;

X_{19} is a hydrophilic amino acid;

X_{20} is a hydrophilic amino acid;

"-" is an amide, a substituted amide or an isostere of amide thereof;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

24. The method of claim 23 wherein:

B_{11} and B_{22} are each independently a peptide of 1-3 amino acids, at least one of which is an aromatic amino acid;

Z_{12} and Z_{21} are each independently a Cys-like amino acid;

X_{13} is absent or an aromatic amino acid;

X_{14} is absent or a polar amino acid;

X_{15} is a basic, polar or apolar amino acid;

X_{16} is a polar amino acid;

X_{17} is absent or an apolar amino acid;

X_{18} is an acidic amino acid;

X_{19} is a polar amino acid;

X_{20} is a basic amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

25. The method of claim 24 wherein:

B_{11} and B_{22} are each independently Tyr or Phe;

Z_{12} and Z_{21} are each Cys;

X_{13} is absent or Phe;

X_{14} is absent or Thr;

X_{15} is Ala, Asn or Arg;

X_{16} is Ser;

X_{17} is absent or Val;

X_{18} is Glu;

X_{19} is Asn;

X_{20} is Arg or His;

"-" is an amide linkage;

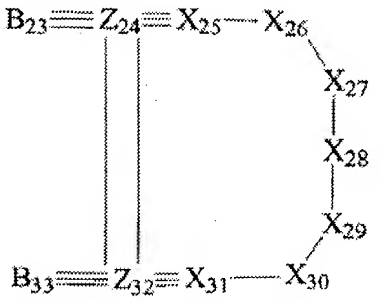
"=" is a disulfide linkage; and

"≡" is an amide linkage.

26. The method of claim 25 wherein the inhibitor is selected from the group consisting of WP5 - SEQ ID NO: 16, WP5N - SEQ ID NO: 17, WP5R - SEQ ID NO: 18, WP5J - SEQ ID NO: 19, WP5JY - SEQ ID NO: 20, WP5JN - SEQ ID NO: 21, WP5JR - SEQ ID NO: 22, and WP5VR - SEQ ID NO: 23.

27. (Amended) The method of claim 18 wherein the compound has the formula:

(IV)



wherein:

B_{23} and B_{33} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_{24} is a moiety of forming a covalent linkage with B_{23}, X_{25} and Z_{32};

Z_{32} is a moiety of forming a covalent linkage with B_{33}, X_{31} and Z_{24};

X_{25} is absent or a hydrophilic amino acid;

X_{26} is a hydrophilic amino acid;

X_{27} is a hydrophilic amino acid;

X_{28} is a hydrophobic amino acid;

X_{29} is a hydrophobic amino acid;

X_{30} is absent or a hydrophobic amino acid;

X_{31} is absent or a hydrophobic amino acid;

"-" is an amide, a substituted amide or an isostere of amide;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

28. The method of claim 27 wherein:

B_{23} and B_{33} are each independently a peptide of 1-3 amino acids, at least one of

which is an aromatic amino acid;

Z_{24} and Z_{32} are each independently a Cys-like amino acid;

X_{25} is absent or a basic amino acid;

X_{26} is a basic amino acid;

X_{27} is an acidic amino acid'

X_{28} is an apolar amino acid;

X_{29} is an apolar amino acid;

X_{30} is absent or a polar amino acid;

X_{31} is absent or an apolar amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

29. The method of claim 28 wherein:

B_{23} and B_{33} are each independently Tyr or Phe;

Z_{24} and Z_{32} are each Cys;

X_{25} is absent or Arg;

X_{26} is Lys;

X_{27} is Glu;

X_{28} is Leu, Pro or Met;

X_{29} is Gly;

X_{30} is absent or Gln;

X_{31} is absent or Val;

"-" is an amide linkage;

"═" is a disulfide linkage; and

"≡" is an amide linkage.

30. The method of claim 29 wherein the inhibitor is selected from the group consisting of WP8L - SEQ ID NO:24.

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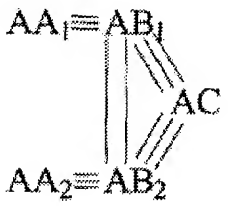
34. (Twice amended) A method of inhibiting bone resorption comprising the step of administering to a patient an amount of an inhibitor effective to inhibit bone resorption, wherein said inhibitor has the formula:



(I)

wherein:

AC is a peptide of 3-18 amino acid residues which corresponds in primary sequence to a binding loop of TNF-R(I), and which may optionally contain one or more amino acid substitutions, or an analogue thereof wherein at least one amide linkage is replaced with a substituted amide or an isostere of amide;

AB_1 is a moiety having a first functional group forming a covalent linkage with one terminus of AC, a second functional group forming a covalent linkage with AB_2 and a third functional group forming a covalent linkage with AA_1 ;

AB_2 is a moiety having a first functional group forming a covalent linkage with the second terminus of AC, a second functional group forming a covalent linkage with AB_1 and a third functional group forming a covalent linkage with AA_2;

AA_1 is a moiety having hydrophobic properties and a functional group forming a covalent linkage with the third functional group of AB_2;

AA_2 is a moiety having hydrophobic properties and a functional group forming a covalent linkage with the third functional group of AB_2;

"$=$" is a covalent linkage; and

"$\equiv$" is a covalent linkage.

35. The method of Claim 34 in which the amino acid substitutions are conservative.

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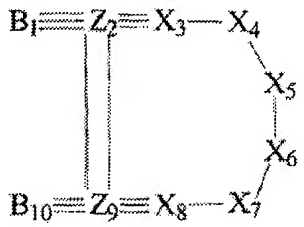
37. (Amended) The method of Claim 36 wherein the inhibitor has the formula:



(II)

wherein:

B_1 and B_{10} are each independently a peptide of 1-6 amino acids at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_2 is a moiety forming a covalent linkage with B_1 , X_3 and Z_9;

Z_9 is a moiety forming a covalent linkage with B_{10}, X_8 and Z_2;

X_3 is absent or a hydrophilic amino acid;

X_4 is a hydrophobic amino acid;

X_5 is a hydrophobic amino acid;

X_6 is a hydrophobic amino acid;

X_7 is a hydrophobic or hydrophilic amino acid;

X_8 is a hydrophobic or hydrophilic amino acid;

"~" is an amide, substituted amide or an isostere of amide thereof;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

38. The method of Claim 37, wherein:

B_1 and B_{10} are each independently a peptide of 1-2 amino acids, at least one of which is an aromatic amino acid ;

Z_2 and Z_9 are each independently a Cys-like amino acid;

X_3 is absent or an acidic amino acid;

X_4 is an aromatic or apolar amino acid;

X_5 is a polar amino acid;

X_6 is a polar amino acid;

X_7 is an aromatic or polar amino acid;

X_8 is an aromatic, apolar or polar amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

39. The method of Claim ~~38~~, wherein:

B_1 and B_{10} are each independently Tyr or Phe;

Z_2 and Z_9 are each Cys;

X_3 is absent or Glu;

X_4 is Trp or Leu;

X_5 is Ser;

X_6 is Gln;

X_7 is Tyr or Asn;

X_8 is Tyr or Leu;

"-" is an amide linkage;

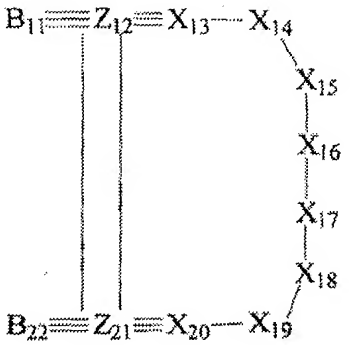
"=" is a disulfide linkage; and

"≡" is an amide linkage.

40. The method of Claim ~~39~~, wherein said inhibitor is selected from the group consisting of WP9Q - SEQ ID NO:13, WP9ELY - SEQ ID NO:12, WP9Y - SEQ ID NO:14, and WP9QY - SEQ ID NO:15.

41. (Amended) The method of Claim 36, wherein the inhibitor has the formula:

(III)



wherein:

B_{11} and B_{22} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_{12} is a moiety forming a covalent linkage with B_{11}, X_{13} and Z_{21};

Z_{21} is a moiety forming a covalent linkage with B_{22}, X_{20} and Z_{12};

X_{13} is absent or hydrophobic amino acid;

X_{14} is absent or hydrophilic amino acid;

X_{15} is a hydrophilic or hydrophobic amino acid;

X_{16} is a hydrophilic amino acid;

X_{17} is absent or a hydrophobic amino acid;

X_{18} is a hydrophilic amino acid;

X_{19} is a hydrophilic amino acid;

X_{20} is a hydrophilic amino acid;

"-" is an amide, a substituted amide or an isostere of amide thereof;

"=" is a covalent linkage; and

"≡" is a covalent linkage.

42. The method of Claim 41, wherein:

B_{11} and B_{22} are each independently a peptide of 1-3 amino acids, at least one of which is an aromatic amino acid;

Z_{12} and Z_{21} are each independently a Cys-like amino acid;

X_{13} is absent or an aromatic amino acid;

X_{14} is absent or a polar amino acid;

X_{15} is a basic, polar or apolar amino acid;

X_{16} is a polar amino acid;

X_{17} is absent or an apolar amino acid;

X_{18} is an acidic amino acid;

X_{19} is a polar amino acid;

X_{20} is a basic amino acid;

"-" is an amide linkage;

"=" is a disulfide linkage; and

"≡" is an amide linkage.

43. The method of Claim 42, wherein:

B_{11} and B_{22} are each independently Tyr or Phe;

Z_{12} and Z_{21} are each Cys;

X_{13} is absent or Phe;

X_{14} is absent or Thr;

X_{15} is Ala, Asn or Arg;

X_{16} is Ser;

X_{17} is absent or Val;

X_{18} is Glu;

X_{19} is Asn;

X_{20} is Arg or His;

"-" is an amide linkage;

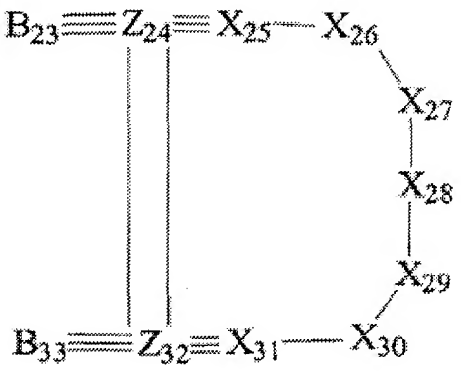
"=" is a disulfide linkage; and

"≡" is an amide linkage.

44. The method of Claim 43, wherein said inhibitor is selected from the group consisting of WP5 - SEQ ID NO:16, WP5N - SEQ ID NO:17, WP5R - SEQ ID NO:18, WP5J - SEQ ID NO:19, WP5JY - SEQ ID NO:20, WP5JN - SEQ ID NO:21, WP5JR - SEQ ID NO:22, and WP5VR - SEQ ID NO:23.

45. (Amended) The method of Claim 36, wherein the inhibitor has the formula:

(IV)



wherein:

B_{23} and B_{33} are each independently a peptide of 1-6 amino acids, at least one of which is a hydrophobic amino acid, an aromatic moiety or a heteroaromatic moiety;

Z_{24} is a moiety forming a covalent linkage with B_{23}, X_{25} and Z_{32};

Z_{32} is a moiety forming a covalent linkage with B_{33}, X_{31} and Z_{24};

X_{25} is absent or a hydrophilic amino acid;

X_{26} is a hydrophilic amino acid;

X_{27} is a hydrophilic amino acid;

X_{28} is a hydrophilic amino acid;

X_{29} is a hydrophilic amino acid;

X_{30} is absent or a hydrophilic amino acid;

X_{31} is absent or a hydrophilic amino acid;

"-" is an amide, a substituted amide or an isostere of amide;

"=" is a covalent linkage; and

"≡" is a covalent linkage.